

**AMENDMENT AND RESPONSE TO OFFICE ACTION**

**Amendment**

**In the Claims**

1. (currently amended) An orally administerable abuse-deterrent pharmaceutical composition comprising

(a) a therapeutically effective amount of a lipophilic drug or lipophilic derivative of a drug prone to abuse, and

(b) a water insoluble formulation comprising carrier materials selected from the group consisting of fats, fatty substances, waxes, wax-like substances and mixtures thereof,

wherein the drug is dispersed within the carrier materials, which prevents the immediate release of a portion of incorporated drug when the physical integrity of the composition is compromised and the resulting material is exposed to water.

2. (currently amended) An orally administerable abuse-deterrent pharmaceutical composition comprising a therapeutically effective amount of a lipophilic derivative of a drug prone to abuse dispersed within one or more carrier materials which are either slowly soluble in water or insoluble in water.

3. (currently amended) The composition of Claim 1 or 2, wherein the composition is a controlled-release pharmaceutical composition.

4. (currently amended) The composition of claim 2 4, wherein the drug is dispersed within the water insoluble carrier materials formulation, and which prevents the immediate release of a substantial portion of incorporated drug when the physical integrity of the composition is compromised and the resulting material is exposed to an aqueous or non aqueous medium water.

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5. (currently amended) The composition of Claim 1 or 4, wherein the portion of the drug released immediately is less than 80% of the total amount of drug incorporated into formulation.

6. (currently amended) The composition of Claim 1 or 2, wherein the composition prevents the immediate release of a substantial portion of incorporated drug when the physical integrity of the composition is compromised and the resulting material is exposed to an aqueous medium.

7. (original) The composition of Claim 6, wherein the portion of the drug released immediately is less than 80% of the total amount of the drug incorporated into the composition.

8. (original) The composition of Claim 1 wherein the drug prone to abuse is selected from the group consisting of 1-phenylcyclohexylamine, 1-piperidinocyclohexanecarbonitrile, alfentanil, alphacetylmethadol, alphaprodine, alprazolam, amobarbital, amphetamine, anileridine, apomorphine, aprobarbital, barbital, barbituric acid derivative, bemedone, benzoylecgonine, benzphetamine, betacetylmethadol, betaprodine, bezitramide, bromazepam, buprenorphine, butabarbital, butalbital, butorphanol, camazepam, cathine, chloral, chlordiazepoxide, clobazam, clonazepam, clorazepate, clotiazepam, cloxazolam, cocaine, codeine, chlorphentermine, delorazepam, dexfenfluramine, dextromoramide, dextropropoxyphen, dezocine, diazepam, diethylpropion, difenoxin, dihydrocodeine, dihydromorphine, dioxaphenetyl butyrate, dipanone, diphenoxylate, diprenorphine, ecgonine, enadoline, eptazocine, estazolam, ethoheptazine, ethyl loflazepate, ethylmorphine, etorphine, fentanyl, fencamfamin, fenfluramine, fentanyl, fludiazepam, flunitrazepam, flurazepam,

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glutethimide, halazepam, haloxazolam, hexalgon, hydrocodone, hydromorphone, isomethadone, hydrocodone, ketamine, ketazolam, ketobemidone, levanone, levoalphacetylmethadol, levomethadone, levomethadyl acetate, levomethorphan, levorphanol, lofentanil, loperamide, loprazolam, lorazepam, lormetazepam, lysergic acid, lysergic acid amide, mazindol, medazepam, mefenorex, meperidine, meptazinol, metazocine, methadone, methamphetamine, methohexitol, methotriimeprazine, methyldihydromorphinone, methylphenidate, methylphenobarbital, metopon, morphine, nabilone, nalbuphine, nalbupine, nalorphine, narceine, nefopam, nicomorphine, nimetazepam, nitrazepam, nordiazepam, normethadone, normorphine, oxazepam, oxazolam, oxycodone, oxymorphone, pentazocine, pentobarbital, phenadoxone, phenazocine, phencyclidine, phendimetrazine, phenmetrazine, pheneridine, piminodine, prodilidine, properidine, propoxyphene, racemethorphan, racemorphan, racemoramide, remifentanil, secobarbital, susfentanil, talbutal, thebaine, thiampylal, thiopental, tramadol, trimeperidine, vinbarbital, allobarbitone, alprazolam, amylobarbitone, aprobarbital, barbital, barbitone, benzphetamine, brallobarbital, bromazepam, brotizolam, buspirone, butalbital, butobarbitone, butorphanol, camazepam, captodiame, carbromal, carfentanil, carpipramine, cathine, chloral, chloral betaine, chloral hydrate, chloralose, chlordiazepoxide, chlorhexadol, chlormethiazole edisylate, chlormezanone, cinolazepam, clobazam, potassium clorazepate, clotiazepam, cloxazolam, cyclobarbitone, delorazepam, dexfenfluramine, diazepam, diethylpropion, difebarbamate, difenoxin, enciprazine, estazolam, ethyl loflazepate, etizolam, febarbamate, fencamfamin, fenfluramine, fenproporex, fluanisone, fludiazepam, flunitraam, flunitrazepam, flurazepam, flutoprazepam, gepirone, glutethimide, halazepam, haloxazolam,

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hexobarbitone, ibomal, ipsapirone, ketazolam, loprazolam mesylate, lorazepam, lormetazepam, mazindol, mebutamate, medazepam, mefenorex, mephobarbital, meprobamate, metaclazepam, methaqualone, methohexital, methylpentynol, methylphenobarbital, midazolam, milazolam, morphine, nimetazepam, nitrazepam, nordiazepam, oxazepam, oxazolam, paraldehyde, pemoline, pentobarbitone, pentazocine, pentobarbital, phencyclidine, phenobarbital, phendimetrazine, phenmetrazine, phenprobamate, phentermine, phenyacetone, pinazepam, pipradol, prazepam, proxibarbal, quazepam, quinalbaritone, secobarbital, secbutobarbitone, sibutramine, temazepam, tetrazepam, triazolam, triclofos, zalepan, zaleplon, zolazepam, zolpidem, and zopiclone.

9. (currently amended) The composition of Claim 1 or 2, wherein the lipophilic derivative of a drug is a free base or a free acid of the drug.

10. (currently amended) The composition of Claim 1 or 2, wherein the lipophilic derivative of a drug is a salt comprising the ionized drug and a lipophilic counter-ion.

11. (currently amended) The composition of Claim 1 or 2, wherein the lipophilic derivative of a drug is a complex comprising one or more components selected from the group consisting of drug molecules, metal cations, and lipophilic counter-ions.

12. (currently amended) The composition of Claim 1 or 2, wherein the lipophilic derivative of a drug is a complex comprising one or more components selected from the group consisting of drug molecules, metal cations, and cyclodextrin molecules.

13. (currently amended) The composition of Claim 1 or 2 wherein the drug is complexed with a metal cation selected from the group consisting of zinc, calcium, magnesium, bismuth and combinations thereof.

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14. (canceled)

15. (currently amended) The composition of Claim 1 or 2, wherein the lipophilic derivative of a drug is a complex comprising the drug and a cyclodextrin.

16. (currently amended) The composition of Claim 1 or 2, wherein the lipophilic derivative of a drug is an ester or amide formed between the drug and a fatty acid.

17. (currently amended) The composition of Claim 4 or 2, wherein the drug is incorporated into a plurality of individual microparticles comprising ~~a~~ the carrier material ~~that is either slowly soluble in water or water insoluble~~.

18. (original) The composition of Claim 17 wherein the microparticles comprise a wax or wax-like material.

19. (original) The composition of Claim 17 wherein the microparticles comprise a fat or a fatty substance.

20. (original) The composition of Claim 17 wherein the microparticles comprise a material selected from the group consisting of naturally water insoluble proteins, naturally water insoluble polysaccharides, naturally water insoluble lipids and phospholipids, cross-linked water soluble proteins, cross-linked water soluble polysaccharides, cross-linked water soluble cyclodextrins and combinations thereof.

21. (original) The composition of Claim 17 wherein the individual microparticles are coated with one or more independent layers, where at least one of the layers is water insoluble and is degraded by enzymes of the human gastrointestinal tract.

22. (original) The composition of Claim 1 wherein the drug is in the form of individual drug particles coated with one or more independent layers where at least one

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of the layers is water insoluble and is degraded by enzymes of the human gastrointestinal tract.

23. (original) The composition of Claim 21 wherein at least one of the layers is water-insoluble, organic solvent-insoluble, and degradable by enzymes present in the human gastrointestinal tract.

24. (canceled)

25. (canceled)

26. (original) The composition of Claim 21 wherein the enzymatically degradable layer(s) comprise a material selected from the group consisting of naturally water insoluble proteins, naturally water insoluble polysaccharides, naturally water insoluble lipids and phospholipids, cross-linked proteins, cross-linked polysaccharides, and combinations thereof.

27. (original) The composition of Claim 1 wherein the drug prone to abuse is co-administered with a drug that has no appreciable abuse potential.

28. (canceled)

29. (currently amended) The composition of claim 1 or 2 wherein the drug prone to abuse is oxycodone.

30-32. (canceled)

33. (currently amended) The composition of Claim 2 wherein the drug prone to abuse is ~~a lipophilic derivative of a drug~~ selected from the group consisting of 1-phenylcyclohexylamine, 1-piperidinocyclohexanecarbonitrile, alfentanil, alphacetylmethadol, alphaprodine, alprazolam, amobarbital, amphetamine, anileridine, apomorphine, aprobarbital, barbital, barbituric acid derivative, bemidone,

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benzoylecgonine, benzphetamine, betacetylmethadol, betaprodine, bezitramide, bromazepam, buprenorphine, butabarbital, butalbital, butorphanol, camazepam, cathine, chloral, chlordiazepoxide, clobazam, clonazepam, clorazepate, clotiazepam, cloxazolam, cocaine, codeine, chlorphentermine, delorazepam, dexfenfluramine, dextromoramide, dextropropoxyphen, dezocine, diazepam, diethylpropion, difenoxin, dihydrocodeine, dihydromorphine, dioxaphenyl butyrate, dipanone, diphenoxylate, diprenorphine, ecgonine, enadoline, eptazocine, estazolam, ethoheptazine, ethyl loflazepate, ethylmorphine, etorphine, fempromponex, fencamfamin, fenfluramine, fentanyl, fludiazepam, flunitrazepam, flurazepam, glutethimide, halazepam, haloxazolam, hexagonal, hydrocodone, hydromorphone, isomethadone, hydrocodone, ketamine, ketazolam, ketobemidone, levanone, levoalphacetylmethadol, levomethadone, levomethadyl acetate, levomethorphan, levorphanol, lofentanil, loperamide, loprazolam, lorazepam, lormetazepam, lysergic acid, lysergic acid amide, mazindol, medazepam, mefenorex, meperidine, meptazinol, metazocine, methadone, methamphetamine, methohexital, methotriimeprazine, methyldihydromorphinone, methylphenidate, methylphenobarbital, metopon, morphine, nabilone, nalbuphine, nalbupine, nalorphine, narceine, nefopam, nicomorphine, nimetazepam, nitrazepam, nordiazepam, normethadone, normorphine, oxazepam, oxazolam, oxycodone, oxymorphone, pentazocine, pentobarbital, phenadoxone, phenazocine, phencyclidine, phendimetrazine, phenmetrazine, pheneridine, piminodine, prodilidine, properidine, propoxyphene, racemethorphan, racemorphan, racemoramide, remifentanil, secobarbital, sufentanil, talbutal, thebaine, thiampylal, thiopental, tramadol, trimeperidine, vinbarbital, allobarbitone, alprazolam, amylobarbitone, aprobarbital, barbital, barbitone,

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benzphetamine, brallobarbital, bromazepam, brotizolam, buspirone, butalbital, butobarbitone, butorphanol, camazepam, captodiame, carbromal, carfentanil, carpipramine, cathine, chloral, chloral betaine, chloral hydrate, chloralose, chlordiazepoxide, chlorhexadol, chlormethiazole edisylate, chlormezanone, cinolazepam, clobazam, potassium clorazepate, clotiazepam, cloxazolam, cyclobarbitone, delorazepam, dexfenfluramine, diazepam, diethylpropion, difebarbamate, difenoxin, enciprazine, estazolam, ethyl loflazepate, etizolam, febarbamate, fencamfamin, fenfluramine, fenproporex, fluanisone, fludiazepam, flunitraam, flunitrazepam, flurazepam, flutoprazepam, gepirone, glutethimide, halazepam, haloxazolam, hexobarbitone, ibomal, ipsapirone, ketazolam, loprazolam mesylate, lorazepam, lormetazepam, mazindol, mebutamate, medazepam, mefenorex, mephobarbital, meprobamate, metaclazepam, methaqualone, methohexital, methylpentynol, methylphenobarbital, midazolam, milazolam, morphine, nimetazepam, nitrazepam, nordiazepam, oxazepam, oxazolam, paraldehyde, pemoline, pentobarbitone, pentazocine, pentobarbital, phencyclidine, phenobarbital, phendimetrazine, phenmetrazine, phenprobamate, phentermine, phenyacetone, pinazepam, pipradol, prazepam, proxibarbal, quazepam, quinalbaritone, secobarbital, secbutobarbitone, sibutramine, temazepam, tetrazepam, triazolam, triclofos, zalepan, zaleplon, zolazepam, zolpidem, and zopiclone.

34. (currently amended) The composition of Claim 1 or 2 wherein the lipophilic derivative is dissolved in the carrier material in a molten state to result in a uniform dispersion within the carrier material.

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35. (currently amended) The composition of Claim 1 or 2 wherein the lipophilic derivative is dissolved in a co-solvent along with a carrier material to result in a uniform dispersion within the carrier material.

36. (currently amended) The composition of Claim 10 wherein the lipophilic counter-ion is selected from the group consisting of stearic acid, palmitic acid, myristic acid, and mixtures thereof.

37. (currently amended) The composition of Claim 1 or 2 comprising one or more excipients selected from the group consisting of stearic acid, palmitic acid, and mixtures thereof.

38. (currently amended) The composition of Claim 1 or 2 comprising one or more excipients selected from the group consisting of beeswax, carnauba wax, hydrogenated oil, and mixtures thereof.

39. (new) The composition of claim 1, wherein the drug is incorporated into a plurality of individual microparticles comprising the carrier material(s).

40. (new) The composition of claim 17 or 39, wherein the individual microparticles are further formulated into a tablet or capsule for oral administration.